UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/446,677 | 03/24/2000 | SVEND BIRKELUND | BIRKELUND=1 | 2720 |

1444 7590 09/26/2003

BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

| EXAMINER |
|---|
| SHAHNAN SHAH, KHATOL S |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1645 | |

DATE MAILED: 09/26/2003

29

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Appli ation No. 09/446,677 | Applicant(s) BIRKELUND ET AL. | |
|---|---|---|---|
| | Examiner Khatol S Shahnan-Shah | Art Unit 1645 | |

*-- Th MAILING DATE of this communication app ars on the cover she t with th correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *08 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-11,13 and 15-44* is/are pending in the application.

4a) Of the above claim(s) *1-4, 6, 8, 9, 11, 13 and 15-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,7,10 and 19-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

***Detailed Action***

**1.** Applicants' amendment E and response received July 08, 2003, paper 27 is acknowledged. Claim 5 was amended. New claims 19-44 were added.

**2.** Currently claims 1-11, 13 and 15-44 are pending.

**3.** Claims 5, 7, 10 and 19-44 are under consideration. Claims 1-4, 6, 8, 9, 11, 13 and 15-18 are withdrawn from consideration as being drawn to non-elected inventions.

***Prior Citations of Title 35 Sections***

**4.** The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior office action.

***Rejections Maintained***

**5.** The rejection of claims 5, 7 and 10 under 35 USC § First Paragraph, made in paragraph 12 of the office action mailed June 03, 2002 (paper number 22) is maintained.
The rejection was as stated below:

Claims 5, 7 and 10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polypeptide of SEQ ID NO: 2, does not reasonably provide enablement for the variants and subsequences claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims are directed to a protein derived from *Chlamydia pneumoniae* having amino acid sequence shown in SEQ ID NO: 2 or a variant or subsequence thereof. The claims are broad and encompass any protein derived from Chlamydia *pneumoniae*. The specification indicates that "a

variant will typically show a sequence similarity of preferably at least 50%, preferably at least 60%, preferably at least 70%, such as at least 80%, e.g. at least 90%, 95%, 98%." (see page 10, lines 10-14). The specification further indicates, " A subsequence will typically comprise at least 100 amino acids, preferably at least 80 amino acids, more preferably at least 70 amino acids, such as 50 amino acids. It might be as small as 10-50..." (see page 10 lines 29-34).

The specification does not provide any description of these variants and which positions in these variants can be altered without loss of protein activity or which position would render a non-functional protein. Furthermore, no examples of any of these variants are provided. No information, beyond the characterization of SEQ ID NO: 2 have been provided by applicant, which would indicate possession of the claimed variants. No description has been provided by applicant of the variants encompassed by the claims. The specification has no disclosure of the function of all of the variants. Each variant and subsequences of the proteins claimed is a large variable genus, which can have a wide variety of functions. The art also teaches functionally unrelated molecules can be produced by these substitutions for example Van de Loo et al. (Proc. Natl. Acad. Sci 1995) teaches that polypeptides of approximately 67% homology to a desaturase from Arabidopsis were found to be hydrolases once tested for activity (see abstract). Similarly, Broun et al. (Science 1998) teaches that as few as four amino acid substitutions can convert an oleate 12-desaturase into a hydrolase and as few as six amino acid substitutions can transform an hydrolase into a desaturase (see abstract). Therefore, many functionally unrelated variants (polypeptides) are encompassed within the scope of the claims.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of variants broadly encompassed by the

claims and the claims broadly encompass a significant number of inoperative species. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and still retain similar activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, the problem of prediction protein structure from mere sequence data of a single protein and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex and well outside the realm of routine experimentation.

One skilled in the art would expect any tolerance to modification shown for a given protein to diminish with each further and additional modification, e.g. Multiple substitutions. The sequence of some proteins is highly conserved and one skilled in the art would not expect tolerance to any amino acids modification in such proteins.

The specification does not support the broad scope of the claims, which encompass all modifications and fragments because the specification does **not** disclose the following:

- the general tolerance to modification and extent of such tolerance;
- specific positions and regions of the sequence(s) which can be predictably modified and which regions are critical;
- what fragments, if any, can be made which retain the biological activity if the intact protein; and

- the specification provide essentially no guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicant have **not** provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed protein in manner reasonably correlated with the scope of the claims broadly including any number of additions, deletions or substitutions and fragments of any size. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970). Without such guidance, the changes which can be made in the proteins structure and still maintain activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Amgen Inc v. Chugai Pharmaceutical Co Ltd. 927 F 2d 1200, 18 USPQ2d 1016 (Fed.Cir.1991) at 18 USPQ2d 1026-1027 and Exparte Forman, 230 U.S.P.Q. 546(Bd. Pat. App. & Int. 1986).

In view of all of the above, in view of the lack of predictability in the art, it is determined that it would require undue experimentation to make and use the invention commensurate in scope with the claims.

Applicants' arguments filed July 08, 2003 have been fully considered and are not persuasive.

Applicants argue " The variants of claim 5 (ii) are required to have an amino acid sequence identity of at least 80% to at least one of isolated proteins of (i), and to compromise at least one epitope of least one of said isolated proteins". Applicants also argue, " Claim 5 is directed to a protein per se, and hence is enabled if there is any use for the claimed proteins".

It is the examiner's position that it seems that the applicants argue utility. The rejection was not a utility rejection but a scope of enablement in regard to the variants and subsequences broadly claimed by the applicants.

It also is the examiner's position that the specification does not reasonably provide enablement for the variants and subsequences in the amended claims. The specification does not provide any description of these variants and which positions in these variants can be altered without loss of protein activity or which position would render a non-functional protein. Furthermore, no examples of any of these variants are provided. In regard to at least one epitope it is not clear from the specification how this "epitope" is elected? It is not clear what could be the common attribute among these epitopes? The claims are drawn to a product or an antigen used in diagnostic assays or as a vaccine as recited by the applicants in page 7 of the response. The art is unpredictable with regard to predicting antigenic determinants from sequences for example Jameson and Wolf (CABIOS, 4 (1): 181-186 1988, prior art of record) in page 185 recite " The use of such algorithm will always have inherent limitations. The user must supply biological considerations, e.g. that cytoplasmically exposed regions of transmemberane proteins will not be recognized by the immune system".

It is also unclear how the amino acid sequences are selected or how the skilled artisan would predict the sequences required to accomplish the required function. The specification does not teach how one would make this selection or teach a method to predetermine the sequence structure for appropriate selection to result in the required affinity constant and antigenic specificity. The art teaches that even minor changes in the amino acid sequences may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc Natl Acad Sci USA 1982 Vol 79 page 1979). Rudikoff et al. teaches that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function (see abstract and title).

In view of the lack of guidance, lack of examples, and lack of predictability associated with regard to producing and using the myriad of derivatives and fragments encompassed in the scope of the claims one skilled in the art would be forced into undue experimentation in order to practice broadly the claimed invention.

In conclusion the specification does not support the broad scope of the claims, which encompass a multitude of analogs or equivalents because the specification does not disclose the following:

-the general tolerance to modification and extent of such tolerance;

-specific positions which can be predictably modified; and

-the specification provides essentially no guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one skilled in the art to make and use the claimed derivatives in a manner reasonably correlated with the scope of the claims broadly including any number of variants. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made and still maintain activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986).

Note: Newly added claims 19-44 also rejected under 112 1st paragraph for the reasons stated above.

**6.** The rejection of claim 5 under 35 USC § 102(b), made in paragraph 14 of the office action mailed June 03, 2002 (paper number 22) is maintained.

The rejection was as stated below:

Claim 5 is rejected under 35 U.S.C. 102(b) as being anticipated by Melgosa et al. (FEMS Microbiology Letters Vol. 112, No. 2, pp. 199-204, September 1993). Prior art already made of record.

Claim 5 is drawn to a protein derived from *Chlamydia pneumoniae* having the amino acid sequence shown in SEQ ID NO: 2 or a variant or subsequence thereof having a sequence similarity of at least 50% and similar biological function.

Melgosa et al. teach a protein derived from *Chlamydia pneumoniae.* Melgosa et al. teach a 98-kDa protein from outer membrane complex of *Chlamydia pneumoniae* (see abstract and page 202). SEQ ID NO: 2 or a variant of the claimed invention will be inherent in the 98-kDa protein taught by Melgosa et al.

Since the office does not have the facilities for examining and comparing applicants' product with the product of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i. e., that the product of prior art does not possess the same material structure and functional characteristics of the claimed product). See In re Best, 562 F.2 d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicants' arguments filed July 08, 2003 have been fully considered and are not persuasive.

Applicants argue " the claim recites an isolated protein and it is evident that Melgosa et al. in fact failed to isolate any of the recited chlamydial proteins".

It is the examiner's position that Melgosa et al. do teach isolated proteins. Melgosa isolated the proteins by extracting of outermembrane proteins from elementary bodies (EBs)

and than the purified proteins were separated by electrophoresis (SDS-page) see page 300.

In conclusion, it is the examiner's position that claim 5 as amended is still drawn to a protein derived from *Chlamydia pneumoniae* having the amino acid sequence shown in SEQ ID NO: 2 or a variant or subsequence thereof having a sequence similarity of at least 80%. The prior teach the claimed protein.

**7.** The rejection of claim 7 under 35 USC § 102(b), made in paragraph 15 of the office action mailed June 03, 2002 (paper number 22) is maintained.

The rejection was as stated below:

Claim 7 is rejected under 35 U.S.C. 102(b) as being anticipated by Melgosa et al. (FEMS Microbiology Letters Vol. 112, No. 2, pp. 199-204, September 1993).

Claim 7 is drawn to a kit for diagnosis of infection of a mammal with *Chlamydia pneumoniae* comprising a protein with the amino acid sequence shown in SEQ ID NO: 2 or a variant or subsequence thereof. (The examiner views the claimed kit as a product or a composition comprising a protein of *Chlamydia pneumoniae*).

Melgosa et al. teach a product or a composition for diagnosis of infection of a mammal with *Chlamydia pneumoniae* comprising a protein derived from *Chlamydia pneumoniae.* Melgosa et al. teach a composition of 98-kDa protein from outer membrane complex of *Chlamydia pneumoniae* (see abstract) This composition was used for diagnosis of Chlamydia *pneumoniae* in rabbits (see page 201). SEQ ID NO: 2 or a variant of the claimed invention will be inherent in the 98-kDa-protein composition taught by Melgosa et al.

Applicants' arguments filed July 08, 2003 have been fully considered and are not persuasive.

Applicants argue " the claim recites an isolated protein and it is evident that Melgosa et al. in fact failed to isolate any of the recited chlamydial proteins".

It is the examiner's position that Melgosa et al. do teach isolated proteins. Melgosa isolated the proteins by extracting of outermembrane proteins from elementary bodies (EBs) and than the purified proteins were separated by electrophoresis (SDS-page) see page 300.

In conclusion, it is the examiner's position that the base claim (claim 5) which claim 7 is depended from is drawn to a protein derived from *Chlamydia pneumoniae* having the amino acid sequence shown in SEQ ID NO: 2 or a variant or subsequence thereof having a sequence similarity of at least 80%. The prior teach the claimed invention.

**8.** The rejection of claim 10 under 35 USC § 102(b), made in paragraph 16 of the office action mailed June 03, 2002 (paper number 22) is maintained.

The rejection was as stated below:

Claim 10 is rejected under 35 U.S.C. 102(b) as being anticipated by Melgosa et al. (FEMS Microbiology Letters Vol. 112, No. 2, pp. 199-204, September 1993).

Claim 10 is drawn to a composition for immunizing a mammal against *Chlamydia pneumoniae* comprising a protein with the amino acid sequence shown in SEQ ID NO: 2 or a variant or subsequence thereof.

Melgosa et al. teach a composition for immunizing a mammal against *Chlamydia pneumoniae* comprising a protein derived from *Chlamydia pneumoniae*. Melgosa et al. teach a composition of 98-kDa protein from outer membrane complex of *Chlamydia pneumoniae* (see

abstract) This composition was used to immunize rabbits (see page 200). SEQ ID NO: 2 or a variant of the claimed invention will be inherent in the 98-kDa-protein composition taught by Melgosa et al.

Since the office does not have the facilities for examining and comparing applicants' product with the product of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i. e., that the product of prior art does not possess the same material structure and functional characteristics of the claimed product). See In re Best, 562 F.2 d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicants' arguments filed July 08, 2003 have been fully considered and are not persuasive.

Applicants argue " the claim recites an isolated protein and it is evident that Melgosa et al. in fact failed to isolate any of the recited chlamydial proteins".

It is the examiner's position that Melgosa et al. do teach isolated proteins. Melgosa isolated the proteins by extracting of outermembrane proteins from elementary bodies (EBs) and than the purified proteins were separated by electrophoresis (SDS-page) see page 300.

In conclusion, it is the examiner's position that the base claim (claim 5) which claim 10 is depended from is drawn to a composition a protein derived from *Chlamydia pneumoniae* having the amino acid sequence shown in SEQ ID NO: 2 or a variant or subsequence thereof having a sequence similarity of at least 80%. The prior teach the claimed protein.

***New Ground for Objections and Rejections***

***Objections to Specification***

**9.** The disclosure is objected to because of the following informalities:

This specification contains sequences in the specification which does not comply to 37 CFR 1.821 (d) for failing to reference to the sequences by use of sequence identifiers, preceded by " SEQ ID NO" in the text of description. Appropriate correction is required.

**10.** The specification page 30 recites the abbreviation "IPTG". Full name of the abbreviation is required when appears for the first time in a disclosure.

### *Claim Objections*

**11.** Claims 27, 28, 29, 30, 34, 36, 37, 38, and 44 are objected to because of the following informalities: These claims do not comply with the sequence rules.

These claims contains sequences, which does not comply to 37 CFR 1.821 (d) for failing to reference to the sequences by use of sequence identifiers, preceded by " SEQ ID NO" in the text of the claims. 37 CFR 1.821 (d) requires that any sequences containing four or amino acid should be reference to by sequence identifiers, preceded by " SEQ ID NO" Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

**12.** The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

**13.** Claims 26, 31, 32, 43 and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 26 recites the abbreviation "PAB150". Full name of the abbreviation is required when appears for the first time in a claim.

Claims 31 and 32 are indefinite because they refer to the figures.

Claim 43 recites: " an apparent molecular, under by SDS-PAGE of 89-101 or 56-57 kDa ". This is indefinite in that the claim does not state if the molecular weights were obtained under reducing or non-reducing conditions. Proteins can exhibit widely differing apparent molecular weight as determined by SDS-PAGE in the absence or presence of thiol groups, therefore the recitation of "molecular weight...(SDS-PAGE)" without further qualifiers, does not set the metes and bounds the claim.

*New Matter Rejection*

**14.** Claims 5, 7, 10 and 19-44 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

Amended claim 5 and new claims 34 and 43 now include the newly added limitation " said protein being free of any other chlamydial protein". However, there appears to be no descriptive support in the instant specification for this added limitation. Applicants are respectfully requested to point out to the proper descriptive support in specific part (s) of the disclosure as filed, for the newly added limitation, or to remove the new matter from the claims.

Specification page 29, line recites that "proteins were partially purified as inclusion bodies", page 30 lines 6-8 recites that " The histidine tagged fusion protein was expressed by induction by the synthesis of IPTG and purified over a nikle column" There is no reference to "protein being free of any other chlamydial protein" anywhere in the specification. It is not clear if partially purified protein is free from any other chlamydial proteins. How far the protein was purified? Applicants' recite in page 6 of the reply "omp4 was produced free of omp 5, 6, 7, 8, 9,

10, 11, 12 and 13. (page 8, lines 21-33)". It is the examiner's position that page 8, lines 21-33 does not recite the said phrase or said concept. 37 CFR 1.121 requires that an amendment to the claim must have antecedent basis in the original disclosure. Therefore the new limitation in the claim is considered new matter. *In re Rasussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step or a compound from a disclosure. See MPEP 608.04.

***Conclusion***

**15.** No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol Shahnan-Shah whose telephone number is (703) 308-8896. The examiner can normally be reached on 7:30 AM - 4 PM from Monday through Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned to is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Khatol Shahnan-Shah, BS, Pharm, MS

Biotechnology Patent Examiner

Art Unit 1645, September 23, 2003

RODNEY P SWARTZ, PH.D
PRIMARY EXAMINER